

PATENT CLAIMS

1. A method of producing a protein variant evoking a lowered immunogenic response in animals including man in comparison to the response evoked by its parent protein, whereby said protein is epitope mapped using immunological and proteochemical methods, epitopes are determined, and at least one of said epitopes is changed through mutation of a DNA molecule coding for the expression of said parent protein or synthesis of a DNA molecule coding for the expression of said variant protein, said mutated or constructed DNA molecule subsequently being inserted into a vector for transformation of transfection into a suitable host, wherein said vector is functional or whereby said mutated or constructed DNA molecule is integrated functionally into the genome of said host, said protein variant is expressed in the host, and recovered.
2. The method of claim 1, wherein said protein is an industrial enzyme.
3. The method of claim 2, wherein said enzyme is a detergent enzyme, such as a protease, lipase, cellulase, amylase, or oxidase.
4. The method of claim 2, wherein said enzyme is a process enzyme, such as an amylase, lyase, lipase, or cellulase.
5. The method of claim 1, wherein said protein is a medicinal protein, such as a hormone, or medicinal enzyme.
6. A protein variant produced by the method of any of the claims 1 to 5.
7. The protein variant of claim 6, selected from the group comprising industrial enzymes, such as detergent enzymes, e.g. proteases, lipases, cellulases, amylases, or

oxidases, process enzymes, e.g. amylases, lyases, lipases, or cellulases.

8. The protein variant of claim 7, wherein said protein is a protease.

9. The protease variant of claim 8, wherein said protease is a subtilisin protease.

10. The protease variant of claim 9, representing a variant of a parent enzyme selected from subtilisin BPN', subtilisin amylosacchariticus, subtilisin 168, subtilisin mesentericopeptidase, subtilisin Carlsberg, subtilisin DY, subtilisin 309, subtilisin 147, thermitase, aqualysin, Bacillus PB92 protease, proteinase K, Protease TW7, and Protease TW3.

11. The protease variant of claim 10, wherein the parent enzyme is subtilisin 309.

12. The protease variant of claim 10, wherein the parent subtilisin is subtilisin 147.

13. The protease variant of claim 10, wherein the parent subtilisin is subtilisin Carlsberg.

14. The protease variant of claim 10, wherein the parent subtilisin is Bacillus PB92 protease.

15. A subtilisin protease variant, wherein the immunological potential has been changed in comparison to the parent protease, for example in that, in said protease changes have been performed among the amino acid residues at any one or more of positions

127, 128, 129, 130, 131, 136, 151, 152, 153, 154, 161, 162, 163, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 186, 193, 194, 195, 196, 197, 247, 251, 261,

by deletion, substitution, or insertion (single or multiple) adjacent to the indicated positions, whereby said subtilisin protease has an immunological potential lower than that of said parent protease.

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16. The protease variant of any of the claims 8 to 15, characterised in that it possesses at least one mutation affecting an amino acid residue occupying a position chosen from the group of positions

10 127, 151, 152, 153, 154, 168, 169, 173, 174, 175, 176, 193, 196.

17. The protease as claimed in any preceding claim, further characterised in that it contains at least one or  
15 more sets of mutations affecting amino acid residues occupying a position chosen from the group of sets of positions:

36+209, 89+120, 136+170, 120+235, 170+195, 36+89, 89+235, 136+195, 181+222, 195+251, 209+222, 235+251.

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18. The protein variant of claim 6, selected from the group comprising medicinal proteins, e.g. hormones, e.g. insulin, HCG, or growth hormone.

25 19. The protein variant of claim 6, selected from the group comprising medicinal enzymes, e.g. factor V, factor VII, factor VIII, or other proteins, e.g. interleukins, or interferons.

30 20. A composition comprising any protein variant according to any of claims 6 to 19.

21. The composition of claim 20, wherein said composition is a detergent compositions.

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22. The composition of claim 20, wherein said composition is a compositions for use in preventive and/or

~~alleviating therapy and/or diagnosis of various conditions in the animal body, including man.~~

23. Use of a protein ~~or composition~~ according to any of 5 the claims 6 to 22 in detergents ~~or for preventive and/or~~ alleviating therapy and/or diagnosis of various conditions in the animal body, including man.

Add A<sup>2</sup>

Add C2

Add D1

Add E1

Add B1

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